



FORM PTO-1449

INFORMATION DISCLOSURE  
STATEMENT

DOCKET NO:

71432/49168 C

SERIAL NO.:

09/932,058

APPLICANT(S): J. Skouv et al.

FILING DATE:

08/16/2001

GROUP NO.:

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## UNITED STATES PATENT DOCUMENTS

EXAM. INITIALS		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
2	AA	4,683,195	07/28/87	Mullis et al.	435	6	
	AB	4,683,202	07/28/87	Mullis	435	91	
	AC	4,800,159	01/24/89	Mullis et al.	435	172.3	
	AD	5,605,794	02/25/97	Rust et al.	435	6	
2	AE	5,432,272	07/11/95	Benner	536	25.3	

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO
12	BA	EP0332435A2	03/09/89	European Patent Application			
1	BB	EP0333465A2	03/15/89	European Patent Application			
1	BC	EP0324474A1	01/12/89	European Patent Application			
1	BD	EP0538194B1	10/08/92	European Patent Application			
1	BE	WO 96/31557	10/10/96	PCT			
1	BF	WO 89/09835	10/19/89	PCT			
1	BG	WO 98/22489	05/28/98	PCT			
1	BH	WO 99/14226	03/25/99	PCT			
2	BI	WO 98/39352	09/11/98	PCT			

## OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)

12	CA	Altman, Karl-Heinz, et al., "1',6'-Methano Carbocyclic Thymidine: Synthesis, X-ray Crystal Structure, and Effect on Nucleic Acid Duplex Stability"; Tetrahedron Letters; 35 (41), 7625-7628, 1994					
12	CB	Altman, Karl-Heinz, et al., "4',6'-Methano Carbocyclic Thymidine: A Conformationally Constrained Building Block for Oligonucleotides"; Tetrahedron Letters; 35 (15), 2331-2334, 1994					
92	CC	Barany, Francis, "Genetic disease detection and DNA amplification using cloned thermostable ligase"; Proc. Natl. Acad. Sci. USA; 88, 189-193, 1991					



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/	CD	Bolli, Martin, et al., "Bicyclo-DNA: a Hoogsteen-selective pairing system"; Chemistry & Biology; 3 (3), 197-206, 1996	
/	CE	Bolli, Martin, et al., "Nucleic-Acid Analogs with Restricted Conformational Flexibility in the Sugar-Phosphate Backbone"; Helvetica Chimica Acta; 78, 2077-2096, 1995	
/	CF	Bolli, Martin, et al., "Triple-Helix Formation of Oligodeoxynucleotides Containing [3'S,5'R]-2'-Deoxy-3',5'-ethano-B-D-ribofuranosyl]nucleosides ("Bicyclo-deoxynucleosides); Angew. Chem. Int. Engl. 34 (6), 1995	
/	CG	Bolli, Martin, et al., "Watson- Crick base-pairing properties of bicyclo-DNA"; Nucleic Acids Research; 24 (23), 4660-4667, 1996	
/	CH	Bos, Johannes L., et al., "Prevalence of ras gene mutations in human colorectal cancers"; Nature; 327, 1987	
/	CI	CHIMIA 36 <sup>th</sup> IUPAC Congress, "Frontiers in Chemistry, New Perspectives for the 2000s"; Geneva, Switzerland, August 17-22, 1997	
/	CJ	Christensen, Nanna, et al., "A Novel Class of Oligonucleotide Analogues Containing 2'-O,3'-C-linked [3.2.0] Bicycloarabinonucleoside Monomers: Synthesis, Thermal Affinity Studies, and Molecular Modeling"; Journal of the American Chemical Society; 120 (22), 5458-5463, 1998	
/	CK	De Mesmaeker, Alain, et al., "Backbone modifications in oligonucleotides and peptide nucleic acid systems"; Current Opinion in Structural Biology, 5, 343-355, 1995	
/	CL	Egli, Martin, et al., "Crystal Structure of a Parallel-Stranded Duplex of a Deoxycytidylyl-(3'-5')-deoxycytidine Analogue Containing Intranucleosidyl C(3')-C(5') Ethylene Bridges"; American Chemical Society; 115, 5855-5856, 1993	
/	CM	Ehlen, Thomas, et al., "Detection of Ras Point Mutations by Polymerase Chain Reaction Using Mutation-Specific, Inosine-Containing Oligonucleotide Primers" Biochemical and Biophysical Research Communications; 160 (2), 441-447, 1989	
/	CN	Ezzitouni, Abdallah, et al., "Conformationally locked carbocyclic nucleosides built on a bicyclo[3.1.0]hexane template with a fixed Southern conformation. Synthesis and antiviral activity"; J. Chem. Soc., Perkins Trans.; 1, 1073-1078, 1997	
/	CO	Forrester, Kathleen, et al., "Detection of high incidence of K-ras oncogenes during human colon tumorigenesis"; Nature; 327, 298-303, 1987	
/	CP	Freier, Susan M., et al., "The ups and downs of nucleic acid duplex stability: structure-stability studies on chemically-modified DNA: RNA duplexes"; Nucleic Acid Research; 25 (22), 4429-4443, 1997	
/	CQ	Gibbs, Richard A., et al., "Detection of single DNA base differences by competitive oligonucleotide priming"; Nucleic Acids Research; 17 (7), 2437-2449, 1989	
/	CR	Haliassos, A., et al., "Detection of minority point mutations by modified PCR technique: a new approach for a sensitive diagnosis of tumor-progression markers"; Nucleic Acids Research; 17 (20), 8093-8099, 1989	



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CS	Haly, Becky, et al., "Conformationally Constrained DNA Mimics: Synthesis of a Novel Cyclopropyl-Amide Linked Dimer"; Synlett; 687-689, 1996		
CT	Herdewijin, Piet, "Targeting RNA with Conformationally Restricted Oligonucleotides"; Liebigs Ann.; 1337-1348, 1996		
CU	Imanishi, Takeshi, et al., "Syntheses and Properties of Novel Conformationally Restrained Nucleoside Analogues"; J. Synth. Org. Chem., Jpn.; 57 (11), 969- 980, 1999		
CV	Jakobsen, Mogens Havsteen, et al., "LNA (Locked Nucleic Acids): A New Class of High Affinity Nucleic Acids With Prime Potential as Antisense and Antigene Agents"; Exiqon		
CW	Jones, Gordon H., et al., "4'-Substituted Nucleosides. 5. Hydroxymethylation of Nucleoside 5'-Aldehydes"; J. Org. Chem., 44 (8), 1309-1317, 1979		
CX	Jones, Robert J., et al., "Oligonucleotides Containing a Covalent Conformationally Restricted Phosphodiester Analog for High-Affinity Triple Helix Formation: The Riboacetal Internucleotide Linkage"; American Chemical Society; 115, 9816-9817, 1993		
CY	Kogan, Scott C., et al., "An Improved Method for Prenatal Diagnosis of Genetic Diseases by Analysis of Amplified DNA Sequences"; The New England Journal of Medicine; 317, (16), 985-991, 1987		
CZ	Koshkin, A.A., et al., "Locked Nucleic Acids as Synthetic RNA Mimics for Effective Complementary Recognition"; XIII International Round Table, "Nucleosides, Nucleotides and Their Biological Applications"; Montpellier, France, September 6-10, 1998		
DA	Koshkin, Alexei A., et al., "LNA (Locked Nucleic Acid): An RNA Mimic Forming Exceedingly Stable LNA: LNA Duplexes"; Journal of the American Chemical Society; 120 (50), 13252-13253, 1998		
DB	Koshkin, Alexei A., et al., "Synthesis of Novel 2', 3'-Linked Bicyclic Thymine Ribonucleosides"; 63 (8), 2778-2781, 1998		
DC	Koshkin, Alexei, et al., "LNA (Locked Nucleic Acid): Synthesis of the Adenine, Cytosine, Guanine, 5-Methylcytosine, Thymine and Uracil Bicyclonucleoside Monomers, Oligomerisation, and Unprecedented Nucleic Acid Recognition"; Tetrahedron; 54, 3607-3630, 1998		
DD	Koshkin, Alexei, et al., "Novel Convenient Synthesis of LNA [2.2.1] Bicyclo Nucleosides"; Tetrahedron Letters; 39, 4381-4384, 1998		
DE	Kumar, Ramesh et al., "Designed Diagnostic Restriction Fragment Length Polymorphisms for the Detection of Point Mutations in ras Oncogenes"; Oncogene Research; 1, 235-241, 1989		
DF	Kumar, Ramesh et al., "The First Analogues of LNA: Phosphorothioate-LNA and Thio-LNA"; Bioorganic & Medicinal Chemistry Letters; 8: 2219-2222, 1998		
DG	KværneØ, Lisbet, et al., "Investigation of restricted backbone conformations as an explanation for the exceptional thermal stabilities of duplexes involving LNA (Locked Nucleic Acid): synthesis and evaluation of abasic LNA"; Chem. Commun.; 657-658, 1999		



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✓	DH	Kwok, S., et al., "Effects of primer- template mismatches on the polymerase chain reaction: Human immunodeficiency virus type 1 model studies"; Nucleic Acids Research; 18, 999-1005, 1989
✓	DI	Larder, Brendan A. et al., "Multiple Mutations in HIV-1 Reverse Transcriptase Confer High-Level Resistance to Zidovudine (AZT)"; Science; 246, 1155-1158, 1989
✓	DJ	Litten, J. Christopher, et al., "Bicyclo-Oligonucleotides with Inverted Configuration t C(5'): Synthesis and Properties"; Bioorganic & Medicinal Chemistry Letters; 5 (12), 1231-1234, 1995
✓	DK	Litten, J. Christopher, et al., "Nucleic-Acid Analogs with Restricted Conformational Flexibility in the Sugar-Phosphate Backbone (Bicyclo-DNA)"; Helvetica Chimica Acta; 79, 1129-1146, 1996
✓	DL	Marquez, Victor E., et al., "Nucleosides with a twist. Can Fixed Forms of Sugar Ring Pucker Influence Biological Activity in Nucleosides and Oligonucleotides"; J. Med. Chem.; 39, 3739-3747, 1996
✓	DM	Meldgaard, M., et al., "LNA (Locked Nucleic Acids): Synthesis and thermal denaturation studies"; XIII International Round Table, "Nucleosides, Nucleotides and Their Biological Applications"; Montpellier, France, September 6-10, 1998
✓	DN	Minasov, George., et al., "Structural Basis of Cleavage by Rnase H of Hybrids of Arabinonucleic Acids and RNA"; Biochemistry; 39, 3525-3532, 2000
✓	DO	Nielsen, Christina B., et al., "The Solution Structure of a Locked Nucleic Acid (LNA) Hybridization to DNA"; Journal of Biomolecular Structure & Dynamics; 17 (2), 175-191, 1999
✓	DP	Nielsen, Katrine E., et al., "Solution Structure of an LNA Hybridized to DNA: NMR Study of the d(CT <sup>+</sup> GCT <sup>+</sup> T <sup>+</sup> CT <sup>+</sup> GC): d(GCAGAAGCAG) Duplex Containing Four Locked Nucleotides"; Bioconjugate Chem.; 11, 228-238, 2000
✓	DQ	Nielsen, Kenneth Due, "Oligonucleotide Analogues Containing 4'-C-(Hydroxymethyl) uridine: Synthesis, Evaluation and Mass Spectrometric Analysis"; Bioorganic & Medicinal Chemistry; 3 (11), 1493-1502, 1995
✓	DR	Nielsen, Kenneth, "Syntese og indbygning af 4'-C-(hydroxymethyl)uridin i oligonucleotider"; Kemsik Institut, Odense Universitet, January, 1995
✓	DS	Nielsen, Poul, et al. "Synthesis and chemoselective activation of phenyl 3,5-di-O-benzyl-2-O,4-C-methylene-1-thio-B-D-ribofuranoside: a key synthon towards a-LNA"; Chem. Commun., 2645-2646,
✓	DT	Nielsen, Poul, et al., "A New Convergent Synthetic Approach Towards a- and B- LNA (Locked Nucleic Acid)"; XIII International Round Table, "Nucleosides, Nucleotides and Their Biological Applications"; Montpellier, France, September 6-10, 1998
✓	DU	Nielsen, Poul, et al., "A New Synthetic Approach Towards a- and B-LNA (Locked Nucleic Acids)"; Nucleosides & Nucleotides; 18 (4&5), 701-702, 1999
✓	DV	Nielsen, Poul, et al., "A novel class of conformationally restricted oligonucleotide analogues: synthesis of 2',3'-bridged monomers and RNA-selective hybridization"; Chemm. Commun.; 825-826, 1997



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<input checked="" type="checkbox"/>	DW	Nielsen, Poul, et al., "Synthesis of 2'-O, 3'-C-linked bicyclic nucleosides and bicyclic oligonucleotides"; J. Chem. Soc., Perkins Trans.; 1, 3423-3433, 1997	
<input checked="" type="checkbox"/>	DX	Obika, Satoshi, et al., "Facile synthesis and conformation of 3'-O,4'-C-methyleneribonucleosides"; Chem. Commun., 2423-2424, 1999	
<input checked="" type="checkbox"/>	DY	Obika, Satoshi, et al., "Preparation and Properties of 2', 5'-Linked Oligonucleotide Analogues Containing 3'-O, 4'-C-Methyleneribonucleosides"; Bioorganic & Medicinal Chemistry Letters; 9, 515-518, 1999	
<input checked="" type="checkbox"/>	DZ	Obika, Satoshi, et al., "Stability and structural features of the duplexes containing nucleoside analogues with a fixed N-type conformation, 2'-O, 4'-C-methyleneribonucleosides"; Tetrahedron Letters; 39, 5401-5404, 1998	
<input checked="" type="checkbox"/>	EA	Obika, Satoshi, et al., "Synthesis of 2'-O,4'-C-Methyleneuridine and -cytidine. Novel Bicyclic Nucleosides Having a Fixed C <sub>3</sub> -endo Sugar Puckering"; Tetrahedron Letters; 26 (50), 8735-8738, 1998	
<input checked="" type="checkbox"/>	EB	Obika, Satoshi, et al., "Synthesis of a conformationally locked AZT analogue, 3'-azido-3'-deoxy-2'-O, 4'-C-methylene-5-methyluridine"; Tetrahedron Letters; 40, 6465-6468, 1999.	
<input checked="" type="checkbox"/>	EC	Obika, Satoshi, et al., "Synthesis of conformationally locked C-nucleosides having a 2, 5-dioxabicyclo [2.2.1] heptane ring system"; Tetrahedron Letters; 41, 215-219, 2000	
<input checked="" type="checkbox"/>	ED	Obika, Satoshi, et al., "Triplex formation by an oligonucleotide containing conformationally locked C-nucleoside, 5-(2-O, 4-C-methylene-B-D-ribofuranosyl) oxazole"; Tetrahedron Letters; 41, 221-224, 2000	
<input checked="" type="checkbox"/>	EE	O-Yang, Counde, et al., "Synthesis of 4'-Cyanothymidine and Analogs as Potent Inhibitors of HIV"; Tetrahedron Letters; 33 (1), 37-40, 1992	
<input checked="" type="checkbox"/>	EF	Pfundheller, Henrick M., et al., "Evaluation of Oligonucleotides Containing Two Novel 2'-O-Methyl Modified Nucleotide Monomers: A 3'-C-Allyl and A 2'-O,3'-C-Linked Bicyclic Derivative" Nucleosides & Nucleotides; 18 (9), 2017-2030	
<input checked="" type="checkbox"/>	EG	Rajwanshi, Vivek K., et al., "LNA stereoisomers: xylo-LNA (B-D-xylo configured locked nucleic acid) and a-L-LNA (a-L-ribo configured Locked nucleic acid)"; Chem. Commun.; 1395-1396, 1999	
<input checked="" type="checkbox"/>	EH	Rajwanshi, Vivek K., et al., "The Eight Stereoisomers of LNA (Locked Nucleic Acid): A Remarkable Family of Strong RNA Binding Molecules"; Angew. Chem. Int.; 39 (9), 1656-1659, 2000	
<input checked="" type="checkbox"/>	EI	Rajwashi, Vivek K., et al., "High-Affinity nucleic acid recognition using 'LNA' (locked nucleic acid, B-D - ribo configured LNA), 'xylo-LNA' (b-D-xylo-LNA) or 'a-L-LNA' (a-L-ribo configured LNA)"; Chem. Commun.; 2073-2074, 1999	
<input checked="" type="checkbox"/>	EJ	Raunkjær, Michael, et al., "Oligonucleotide analogues containing (2''S)- and (2''R)-2'-O,3'-C-((2''-C-hydroxymethyl)ethylene)-linked bicyclic nucleoside monomers: Synthesis, RNA-selective binding, and diastereoselective formation of a very stable homocomplex based on T:T base pairing"; J. Chem. Soc. Perkins Trans.; 1, 2543-2551, 1999	



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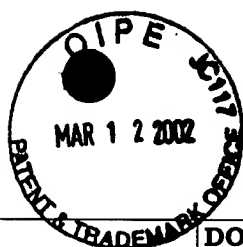
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K	EK	Singh, Janjay K., et al., "Synthesis of 2'-Amino-LNA: A Novel Conformationally Restricted High-Affinity Oligonucleotide Analogue with a Handle"; The Journal of Organic Chemistry; 63 (26), 10035-10039, 1998
1	EL	Singh, Sanjay K., et al., "Synthesis of Novel Bicyclo[2.2.1] Ribonucleosides: 2'-Amino- and 2'-Thio-LNA Monomeric Nucleosides"; The Journal of Organic Chemistry; 63 (18), 6078-6079, 1998
1	EM	Singh, Sanjay K., et al., "Universality of LNA-mediated high-affinity nucleic acid recognition"; Chem. Commun.; 1247-1248, 1998
	EN	Singh, Sanjay, et al., "LNA (locked nucleic acids): synthesis and high-affinity nucleic acid recognition"; Chem. Commun.; 455-456, 1998
1	EO	Soria, Luis F., "Association between a specific apolipoprotein B mutation and familial defective apolipoprotein B-100"; Proc. Natl. Acad. Sci. USA; 86, 587-591, 1989
36	EP	Tarköy, Markus, et al., "Nucleic-Acid Analogues with Constraint Conformational Flexibility in the Sugar-Phosphate Backbone (Bicyclo-DNA)" Helvetica Chimica Acta; 76, 481-510, 1993
	EQ	Tarköy, Markus, et al., "Nucleic-Acid Analogues with Restricted Conformational Flexibility in the Sugar-Phosphate Backbone (Bicyclo-DNA)" Helvetica Chimica Acta; 77, 1994
1	ER	Tarköy, Markus, et al., "Synthesis and Pairing Properties of Decanucleotides from (3'S,5'R)-2'-Deoxy-3',5'-ethano-B-L-ribofuranosyladenine and -thymine"; Angew. Chem. Int. Ed. Engl.; 32 (10), 1993
1	ES	Thrane, Henrik, et al., "Novel Linear and Branched Oligodeoxynucleotide Analogues Containing 4'-C-(Hydroxymethyl) thymidine"; Tetrahedron; 51 (37), 1995
	ET	Tybjaerg-Hansen Anne, "Familial defective apolipoprotein B-100: a single mutation that causes hypercholesterolemia and premature coronary artery disease"; Atherosclerosis; 96, 91-107, 1992 ✓
1	EU	Wahlestedt, Claes, et al., "Potent and nontoxic antisense oligonucleotides containing locked nucleic acids"; PNAS; 97 (10), 5633-5638, 2000
1	EV	Wang, Guangyi, et al., "Conformationally Locked Nucleoside Analogs. Synthesis of 2'-Deoxy-2'-C,4'-C-Bridged Bicyclic Nucleosides"; XIII International Round Table, "Nucleosides, Nucleotides and Their Biological Applications"; Montpellier, France, September 6-10, 1998
1	EW	Wang, Guangyi, et al., "Conformationally Locked Nucleosides. Synthesis and Hybridization Properties of Oligodeoxynucleotides Containing 2', 4'-C-Bridged 2'-Deoxynucleosides"; Bioorganic & Medicinal Chemistry Letters; 9, 1147-1150, 1999
1	EX	Wang, Jianying, et al., "The Synthesis and Binding Properties of Oligonucleotide Analogs Containing Diastereomerically Pure Conformationally Restricted Acetal Linkages"; Bioorganic & Medicinal Chemistry Letters; 7 (2), 229-232, 1997
12	EY	Wengel, Jesper, "Synthesis of 3'-C- and 4'-C-Branched Oligodeoxynucleotides and the Development of Locked Nucleic Acid"; Accounts of Chemical Research; 32 (4), 301-310, 1999

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EZ	Wengel, Jesper, et al., "LNA (Locked Nucleic Acid)"; Nucleosides & Nucleotides; 18 (6&7), 1365-1370, 1999
FA	Wood, William I., et al., "Base composition-independent hybridization in tetramethylammonium chloride: A method for oligonucleotide screening of highly complex gene libraries"; Proc. Natl. Acad. Sci. USA; 82, 1585-1588, 1985.
FB	Wu, Dan Y., et al., "The Litigation Amplification Reaction (LAR)- Amplification of Specific DNA Sequences Using Sequential Rounds of Template-Dependent Litigation"; Genomics; 4, 560-569, 1989
FC	Yannopoulos, Constantin G., et al., "2',3'-Cyclopropanated Nucleoside Dimers"; Synlett; 378-380, 1997
FD	Youssefyeh et al., "Substituted Nucleosided Nucleosides. Synthesis of Some Hydroxymethyl of Nucleosides"; J. Org. Chem.; 44 (8) 1301-1308, 1979
FE	Zou, Ruiming, et al., "Synthesis and Hybridization Properties of an Oligonucleotide Analog Containing a Glucose-derived Conformation-restricted Ribose Moiety and 2',5' Formacetal Linkages"; Tetrahedron Letters; 37 (7), 941-944, 1996

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